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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,887	07/30/2002	Jurgen Engel	103832-512-NP	6290

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Goodwin Procter LLP
599 Lexington Avenue
New York, NY 10022

EXAMINER	
HISSONG, BRUCE D	
ART UNIT	PAPER NUMBER
1646	
MAIL DATE	DELIVERY MODE
09/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/748,887	ENGEL ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4 and 7-16* is/are pending in the application.

4a) Of the above claim(s) *7-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4 and 12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/6/07, 6/12/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. The Applicants' response to the office action mailed on 9/15/2006, including arguments/remarks and amended claims, was received on 6/12/2007 and has been entered into the record.

2. Claims 1-2, 4, and 7-16 are currently pending. Claims 7-11 are withdrawn as non-elected subject matter, and claims 1-2, 4, and 12-16 are the subject of this office action.

Information Disclosure Statement

1. The information disclosure statement received on 2/6/2007 has been considered by the Examiner. Citations 10-12 have been considered. However, if Applicants intend for these citations to be printed, Applicants should resubmit these citations with identifying application numbers and publication dates. Furthermore, citation 9 has been considered in regards to the abstract only, as the remainder of the document is not in English.

2. The information disclosure statement received on 6/12/2007 has been considered by the Examiner. However, the information disclosure statement received on 3/14/2007 has not been considered because it is a duplicate of the 6/12/2007 submission.

Specification

Objection withdrawn

Objection to the specification for being in improper format, as set forth on pages 2-4 of the office action mailed on 9/15/2006, is *withdrawn* in response to Applicants' amendments to the specification.

Objection necessitated by amendment

The amendment filed 7/27/2005 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

Page 1, line 25 of the amended specification recites amino acid sequences for Cetrorelix, Teverelix, Iturelix, and Abrelix. The originally filed specification does not discuss sequence information for these compounds, nor does it disclose references or information that would indicate that these are the only known sequences for the recited compounds.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

Claims 12-16 are objected to for depending from cancelled claims. Claims 12-16 recite the method of any of claims 1-6. However, Applicants have cancelled claims 3 and 5-6.

Claim Rejections - 35 USC § 112, first paragraph – enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection withdrawn

Rejection of claims 1-2, 4, and 12-16 under 35 USC § 112, first paragraph, regarding lack of enablement for a method of lowering sex hormone levels in a human subject by administration of any non-peptide LHRH antagonist, as set forth on pages 5-6 of the prior office action mailed on 9/15/2006, is *withdrawn* in response to Applicants' deletion of the limitation "non-peptide" from the claims.

Rejection maintained

Claims 1-2, 4, and 12-16 *remain rejected* under 35 USC § 112, first paragraph, regarding lack of enablement for determining or defining a subject in need of treatment, and lack

of enablement for method for decreasing T cell populations, as set forth on pages 4-5 of the prior office action mailed on 9/16/2006.

In the response received on 6/12/2007, the Applicants do not appear to have addressed this rejection, and therefore the rejection is maintained.

Claim Rejections - 35 USC § 112, first paragraph – written description

Rejection of claims 1-2, 4, and 12-16 under 35 USC § 112, first paragraph, regarding lack of written description for the claimed genus of non-peptide LHRH antagonists, as set forth on pages 6-7 of the prior office action mailed on 9/15/2006, is *withdrawn* in response to Applicants' amendments to the claims to delete the limitation "non-peptide".

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Rejection of claims 14-16 under 35 USC § 112, second paragraph, as being indefinite for lacking essential method steps, as set forth on page 8 of the prior office action mailed on 9/15/2006, is *withdrawn* in response to Applicants' amendments to the claims to recite "optionally repeating said method of lowering sex hormones".

2. Rejection of claims 12-13 and 15-16 under 35 USC § 112, second paragraph, as being indefinite regarding the recitation of trademarks, as set forth on pages 8-9 of the prior office action mailed on 9/15/2006, is *withdrawn* in response to Applicants' arguments that cetrorelix, teverelilx, and iturelix are non-proprietary, international names for the trademarked CETROTIDE, ANTARELIX, and ANTIDE, respectively, and the amendments to the claims to delete the trademark ANTIDE.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-2 and 12-16 *remain rejected* under 35 USC § 102(b) as being anticipated by Engel et al ("Engel" – WO 98/10781), as set forth on pages 9-10 of the office action mailed on 9/15/2006, and pages 5-6 of the office action mailed on 11/24/2004.

In the response received on 6/12/2007, the Applicants argue that Engel fails to teach or suggest, either expressly or inherently, each and every limitation of the claimed invention as amended because Engel does not disclose the ability of LHRH antagonists to modify T-cell populations. The Applicants also argue that the rejection, as previously set forth, was speculative and conclusory with regards to inherent properties of LHRH antagonists, and that independent claim 1 has been narrowed by including the limitation of "lowered sex hormone levels in said subject result in modification of the T-cell population in said subject."

These arguments have been fully considered and are not persuasive. As set forth previously, Engel teaches administration of the LHRH antagonist cetrorelix, including administration of cetrorelix at doses within the claimed dosage ranges, wherein said administration did not lower sex hormone levels below the level of castration. The previous office action also clearly set forth the teachings of Zakharova *et al* regarding the ability of LHRH antagonists to modify T cell populations. Based on teachings such as Zahkarova *et al*, a person of ordinary skill in the art would recognize that administration of LHRH antagonists, such as cetrorelix, for the purpose of lowering levels of sex hormones, would necessarily also modify T cell populations. Furthermore, it is noted that the claims do not set forth any specific limitations regarding the type or degree of "modification" of T cell populations. Thus, any qualitative or quantitative change in any T cell population would be a "modification of a T cell population". Even in the absence of knowledge of the teachings of Zakharova *et al*, a person of skill in the art would recognize that altering sex hormone levels by administration of LHRH antagonists, as taught by Engel, would have some effect, to some degree, on a T cell population. Therefore, in the absence of specific evidence that the method of administration of an LHRH antagonist (cetrorelix) for lowering sex hormones, as taught by Engel, would not also result in any

modification of any T cell population, the disclosure of Engel anticipates the limitations of the instant claims.

2. Claims 1-2 *remain rejected* under 35 USC § 102(b) as being anticipated by Zakharova et al ("Zakharova"), as set forth on page 10 of the office action mailed on 9/15/2006, and page 6 of the office action mailed on 11/24/2006.

In the response received on 6/12/2007, the Applicants argue that the rejection over Zahkarova, as previously set forth, was speculative and conclusory with regards to inherent properties of LHRH antagonists, and that independent claim 1 has been narrowed by including the limitation of "lowered sex hormone levels in said subject result in modification of the T-cell population in said subject."

These arguments have been fully considered and are not persuasive. As set forth previously, Zakharova teaches administration of LHRH antagonists, and that administration of LHRH antagonists modifies T cell populations by decreasing thymocyte proliferation. While Zahkarova does not specifically teach decreasing sex hormone levels, both Engel (see above) and Gonzalex-Barcena *et al* (see previous office action), clearly teach that administration of LHRH antagonists results in decreased levels of sex hormones. Thus, ordinary skill in the art would recognize that administration of LHRH antagonists for the purpose of modifying T cell populations would also necessarily result in decreased levels of sex hormones. In the absence of specific evidence that the method of administration of an LHRH antagonist for modifying T cell populations, as taught by Zakharova, would not also result in lowering of sex hormone levels, the disclosure of Zakharova anticipates the limitations of the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 4, and 12-16 *remain rejected* under 35 USC § 103(a) as being obvious in view of the combination of Engel *et al* ("Engel"), Zakharova *et al* "Zakharova"), and Jacobson *et al* ("Jacobson"), as set forth on pages 10-11 of the office action mailed on 9/15/2006.

In the response received on 6/12/2007, the Applicants argue Engel is not relevant because "benign prostate hyperplasia" is no longer a limitation of the claims, and because Engel provides no motivation or suggestion to use LHRH antagonists as a treatment to lower sex hormone levels. Therefore, there is no motivation to combine Engel with Zakharova and Jacobson to practice a method of administering LHRH antagonists to lower sex hormone levels.

These arguments have been fully considered and are not persuasive. As set forth *supra*, Engel discloses that administration of LHRH antagonists, at the claimed doses, results in lowering of sex hormone levels (see Fig. 1 and page 8, lines 6-8), and thus provides motivation for administration of LHRH antagonists for lowering of sex hormone levels. Furthermore, the combined teachings of Engel and Zahkarova show that administration of LHRH antagonists results in lowering of sex hormone levels and decreased thymocyte proliferation, respectively, while Jacobson shows that administration of LHRH antagonists is effective in the treatment of autoimmune disease. Thus, a person of ordinary skill in the art, based on the combined teachings of Engel, Zahkarova, and Jacobson, would be motivated to treat autoimmune disease by a method of lowering sex hormones and modifying T cell populations by administration of LHRH antagonists because the skilled artisan would know that LHRH antagonist administration is effective in treating autoimmune disease, can decrease T cell activity, and would know of effective LHRH antagonist doses. For these reasons, the claims of the instant invention are obvious in view of the combination of Engel, Zakharova, and Jacobson.

Conclusion

No claim is allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

/Robert S. Landsman/
Primary Examiner, Art Unit 1647